



DEPARTMENT OF THE AIR FORCE
59TH MEDICAL WING (AETC)
JOINT BASE SAN ANTONIO - LACKLAND TEXAS

21 MAR 2016

MEMORANDUM FOR SGVT

ATTN: MAJ THOMAS BEACHKOFISKY

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your paper, entitled **Genetic and Epigenetic Biomarkers of Cutaneous Adverse Drug Reactions** presented at **Vanderbilt University Dermatology Grand Rounds, TN 7 April 2016** with MDWI 41-108, and has been assigned local file #**16133**.
2. Pertinent biographic information (name of author(s), title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.
3. Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are 59 MDW staff member, we can forward your request for funds to the designated wing POC.
4. Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

Linda Steel-Goodwin

LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

1. TO: CLINICAL RESEARCH		2. FROM: (Author's Name, Rank, Grade, Office Symbol) Thomas Beachkofsky, Maj, O-4, SGO		3. GME/GHSE STUDENT: <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO		4. PROTOCOL NUMBER: N/A	
5. PROTOCOL TITLE: (NOTE: For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.) N/A							
6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED: Genetic & Epigenetic Biomarkers of Cutaneous Adverse Drug Reactions							
7. FUNDING RECEIVED FOR THIS STUDY? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO FUNDING SOURCE:							
8. DO YOU NEED FUNDING SUPPORT FOR PUBLICATION PURPOSES: <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO							
9. IS THIS MATERIAL CLASSIFIED? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO							
10. IS THIS MATERIAL SUBJECT TO ANY LEGAL RESTRICTIONS FOR PUBLICATION OR PRESENTATION THROUGH A COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENT (CRADA), MATERIAL TRANSFER AGREEMENT (MTA), INTELLECTUAL PROPERTY RIGHTS AGREEMENT ETC.? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO NOTE: If the answer is YES then attach a copy of the Agreement to the Publications/Presentations Request Form.							
11. MATERIAL IS FOR: <input checked="" type="checkbox"/> DOMESTIC RELEASE <input type="checkbox"/> FOREIGN RELEASE CHECK APPROPRIATE BOX OR BOXES FOR APPROVAL WITH THIS REQUEST. ATTACH COPY OF MATERIAL TO BE PUBLISHED/PRESENTED.							
<input type="checkbox"/> 11a. PUBLICATION/JOURNAL (List intended publication/journal.)							
<input type="checkbox"/> 11b. PUBLISHED ABSTRACT (List intended journal.)							
<input type="checkbox"/> 11c. POSTER (To be demonstrated at meeting: name of meeting, city, state, and date of meeting.)							
<input checked="" type="checkbox"/> 11d. PLATFORM PRESENTATION (At civilian institutions: name of meeting, state, and date of meeting.) Vanderbilt University Dermatology Grand Rounds, TN, 7 Apr 2016							
<input type="checkbox"/> 11e. OTHER (Describe: name of meeting, city, state, and date of meeting.)							
12. EXPECTED DATE WHEN YOU WILL NEED THE CRD TO SUBMIT YOUR CLEARED PRESENTATION/PUBLICATION TO DTIC NOTE: All publications/presentations are required to be placed in the Defense Technical Information Center (DTIC).							
DATE 18 March 2016							
13. 59 MDW PRIMARY POINT OF CONTACT (Last Name, First Name, M.I., email) Beachkofsky, Thomas, M, thomas.beachkofsky@us.af.mil						14. DUTY PHONE/PAGER NUMBER 210-594-1636	
15. AUTHORSHIP AND CO-AUTHOR(S) List in the order they will appear in the manuscript.							
LAST NAME, FIRST NAME AND M.I.		GRADE/RANK		SQUADRON/GROUP/OFFICE SYMBOL		INSTITUTION (If not 59 MDW)	
a. Primary/Corresponding Author Thomas Beachkofsky		O-4/Maj		59MDW/SGO			
b.							
c.							
d.							
e.							
f.							
I CERTIFY ANY HUMAN OR ANIMAL RESEARCH RELATED STUDIES WERE APPROVED AND PERFORMED IN STRICT ACCORDANCE WITH 32 CFR 219, AFMAN 40-401 JP, AND 59 MDWI 41-108. I HAVE READ THE FINAL VERSION OF THE ATTACHED MATERIAL AND CERTIFY THAT IT IS AN ACCURATE MANUSCRIPT FOR PUBLICATION AND/OR PRESENTATION.							
16. AUTHOR'S PRINTED NAME, RANK, GRADE Thomas Beachkofsky, Maj, O-4				17. AUTHOR'S SIGNATURE BEACHKOFSKY, THOMAS, MARS HALL 1240764284 <small>Signature must be legible and in ink. Do not use a stamp or a computer-generated signature. Date: 20160311 11:10:00 AM</small>		18. DATE 11 March 2016	
19. APPROVING AUTHORITY'S PRINTED NAME, RANK, TITLE Mark Ervin, Col, Chief Operational Medicine				20. APPROVING AUTHORITY'S SIGNATURE ERVIN, MARK, D. 1065325370 <small>Signature must be legible and in ink. Do not use a stamp or a computer-generated signature. Date: 20160311 11:10:00 AM</small>		21. DATE 11 March 2016	

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1st ENDORSEMENT (59 MDW/SGVU Use Only)

TO: Clinical Research Division 59 MDW/CRD Contact 292-7141 for email instructions.		22. DATE RECEIVED 3/14/2016	23. ASSIGNED PROCESSING REQUEST FILE NUMBER 16133
24. DATE REVIEWED 17 Mar 2016		25. DATE FORWARDED TO 502 ISG/JAC	
26. AUTHOR CONTACTED FOR RECOMMENDED OR NECESSARY CHANGES: <input checked="" type="checkbox"/> NO <input type="checkbox"/> YES If yes, give date. _____ <input type="checkbox"/> N/A			
27. COMMENTS <input checked="" type="checkbox"/> APPROVED <input type="checkbox"/> DISAPPROVED The presentation is approved.			
28. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER Rocky Calcote, PhD, Clinical Research Administrator		29. REVIEWER SIGNATURE CALCOTE ROCKY.D.1178245844 <small>Digital signed by: ROCKY.D. CALCOTE DN: cn=Rocky.D. Calcote, ou=59 MDW, ou=USAF Date: 2016.03.17 09:58:44Z</small>	30. DATE

2nd ENDORSEMENT (502 ISG/JAC Use Only)


31. DATE RECEIVED 17 March 2016		32. DATE FORWARDED TO 59 MDW/PA 17 March 2016	
33. COMMENTS <input checked="" type="checkbox"/> APPROVED (In compliance with security and policy review directives.) <input type="checkbox"/> DISAPPROVED Contains the appropriate disclaimer.			
34. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER Arlene Christilles, GS-14, Chief of Civil Law		35. REVIEWER SIGNATURE <i>Arlene Christilles</i>	36. DATE 3/17/16

3rd ENDORSEMENT (59 MDW/PA Use Only)

37. DATE RECEIVED 18 March 2016		38. DATE FORWARDED TO 59 MDW/SGVU 18 March 2016	
39. COMMENTS <input checked="" type="checkbox"/> APPROVED (In compliance with security and policy review directives.) <input type="checkbox"/> DISAPPROVED			
40. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER Christopher Carwile, TSgt/E-6, NCOIC, PA		41. REVIEWER SIGNATURE CARWILE CHRISTOPHER STEWART.1280477229 <small>Digital signed by: CHRISTOPHER STEWART DN: cn=CHRISTOPHER STEWART, ou=59 MDW, ou=USAF Date: 2016.03.21 08:53:24Z</small>	42. DATE 18 March 2016

4th ENDORSEMENT (59 MDW/SGVU Use Only)

43. DATE RECEIVED		44. SENIOR AUTHOR NOTIFIED BY PHONE OF APPROVAL OR DISAPPROVAL <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> COULD NOT BE REACHED <input type="checkbox"/> LEFT MESSAGE	
45. COMMENTS <input type="checkbox"/> APPROVED <input type="checkbox"/> DISAPPROVED			
46. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER		47. REVIEWER SIGNATURE	48. DATE



Genetic & Epigenetic Biomarkers of Cutaneous Adverse Drug Reactions

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Cutaneous Adverse Drug Reactions

- Morbilliform eruption
- Immunobullous
- Acute generalized exanthematous pustulosis (AGEP)
- Serum sickness-like reactions (SSLR)
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
- Drug induced hypersensitivity syndrome (DIHS)
- Erythema multiforme
- Stevens Johnson syndrome
- Toxic epidermal necrolysis

Disclaimer

- The views expressed are those of the [author(s)] [presenter(s)] and do not reflect the official views or policy of the Department of Defense or its Components"

Types of Reactions

- Type 1: (concentration-dependent)
 - Enzymes for drug absorption, distribution, metabolism, excretion (ADME)
 - CYP2C9, CYP2C19, CYP2D6
- Type 2: (idiosyncratic)
 - Major histocompatibility complex II antigens
 - Inflammatory pathways
- Other considerations
 - Epigenetic programming
 - Hereditary
 - Affected by environment (other drugs, infectious agents, smoke, chemicals, stress, hormones)

Adverse Drug Reactions

- 2-15% hospitalized patients
- Leads to 3-6.5% of all hospitalizations
- >100,000 deaths per year in USA
- #6 most common cause of death
- 5-9% of hospital admission costs
- Drug induced skin injury (DISI) is the most common presentation for ADRs

A few known associations...

- Immunologic
 - HLA-B*57:01 and Abacavir
 - HLA-B*15:02 SJS/TEN due to CBZ (Asian pop)
 - HLA-B*58:01 SJS/TEN due to allopurinol (Asian pop)
- Non-immunologic
 - CYP2C19*2 SJS/TEN due to CBZ (Thai children)
 - CYP2C9*3 SJS/TEN due to phenytoin (Asian pop)

Trends

- Genome-wide association studies (GWAS) for ADRs require smaller samples sizes than GWAS for common disease
- Increasing associations with loci outside of the MHC region
- Variants located in noncoding areas of the DNA
- Increasing importance of understanding epigenetic influence

Goals

- Complex:
Discover epigenetic patterns responsible for ADRs through elucidation of epigenomes in relation to transcriptomes under different conditions.
- Simple:
Identify a screenable biomarker associated with increased incidence of cutaneous ADR as to guide medication selection (personalized medicine)

Selected References

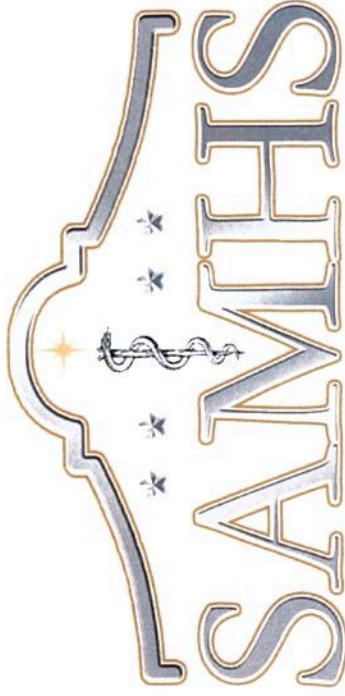
Borroni RG. Pharmacogenetic markers of severe cutaneous adverse drug reactions. *G Ital Dermatol Venereol*. 2014;149:219-26.

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Chan SL. Progress in understanding the genomic basis for adverse drug reactions: a comprehensive review and focus on the role of ethnicity. *Pharmacogenomics*. 2015 May 15:1-19.

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San Antonio Military Health System



Joint Base San Antonio, Texas

Genetic & Epigenetic Biomarkers of Cutaneous Adverse Drug Reactions

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